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Comparison of clinical categories, blood biomarkers and cycle threshold value in COVID-19

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Abstract
Aim: The aim of this study is to investigate whether the viral load of SARS-CoV-2 is an important factor in predicting disease severity and its relationship with clinical and biochemical parameters.
Material and Methods: In this cross-sectional retrospective study, 85 patients who were found to be positive for SARS-CoV-2 PCR at Balıkesir University Health Practice and Research Hospital were evaluated. RT-PCR (CT) values, laboratory values and demographic and clinical data of the patients at the first admission to the hospital were obtained from the electronic environment and compared.
Results: In our study, no significant relationship was found between baseline values and severity of clinical stages in adults with COVID-19. No correlation was found between the gender, vital status, hospitalization or admission to the intensive care unit, presence of comorbidity, degree of disease according to the thorax CT image and mean CT values of the participants included in the study ($p>0.05$).
Discussion: More prospective studies and additional data are needed to determine whether CT values can benefit clinicians in clinical and patient management decisions.

Keywords
Cycle Threshold, COVID-19, Biomarkers

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Introduction

The coronavirus disease (COVID-19) pandemic caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) has spread worldwide at an unprecedented rate after it was first detected in China in December 2019. The gold standard for molecular method for the diagnosis of COVID-19 is the detection of the SARS-CoV-2 virus in respiratory tract samples (nasal, pharyngeal swab or deep tracheal samples) by real-time reverse transcription polymerase chain reaction (RTPCR) [1].

Real-time RT-PCR cycle threshold (CT) values are an indirect method for measuring the copy number of viral RNA. This value represents the number of amplification cycles required for the target gene to exceed a threshold level. CT values are therefore inversely related to viral load [2,3].

Predicting the probable prognosis of patients at the time of diagnosis will greatly assist in patient management decisions [4].

Advanced age and comorbid diseases have been associated with the clinical course of the prognosis of COVID-19 in the literature. Among them, advanced age is an important predictor of mortality [5,6].

If there is a relationship between viral load and disease severity, this relationship may provide additional information on determining the prognosis, whether the patient will be hospitalized or treated on an outpatient basis.

The aim of this study is to investigate whether the viral load of SARS-CoV-2 is an important factor in predicting disease severity and its relationship with clinical and biochemical parameters.

Material and Methods

In this cross-sectional retrospective study, 85 patients who were found to be positive for SARS-CoV-2 PCR in Balıkesir University Health Practice and Research Hospital between 01/01/2020 and 01/10/2021 were evaluated. PCR-negative patients were excluded from the study. CDC has divided patients with COVID-19 according to their clinical stage as mild, moderate, severe and critical. In our study, we divided the patient groups into 2 groups into mild/moderate and severe/critical according to the clinical staging of CDC. 1) Mild group: with mild clinical symptoms without signs of pneumonia on imaging; moderate group: classified as adults with fever and respiratory symptoms with signs of pneumonia on imaging. 2) Severe group was classified as adults with any of the following symptoms: dyspnea, respiratory rate ≥30 breaths/minute or oxygen saturation SpO2≤93% or arterial partial pressure of oxygen ðPaO2Þ/oxygen concentration FiO2Þ≤300mmHg; >50% significant lesion progression within 24-48 hours on pulmonary imaging; Critical group: a group of patients who had respiratory failure and need mechanical ventilation or who are in a state of shock, or need intensive care unit with other organ failures [7].

RT-PCR (CT) values, biochemical parameters and demographic and clinical data of the patients at their first admission to the hospital were obtained from the electronic environment.

RT-PCR, (CT) values and clinical stages of patients were compared in nasal and pharyngeal swabs and deep tracheal aspirate (DTA) samples.

Statistics

All statistical analyzes were performed with IBM SPSS Statistics software (version 26.0). For descriptive data, mean, standard deviation were used for continuous data with a normal distribution; Median, minimum, and maximum values were used for continuous data that did not fit the normal distribution. Student's T-test was used in univariate analyzes for the COVID-19 virus cycle threshold (CT) value, which is continuous data with a normal distribution. Pearson's correlation analysis was performed between the COVID-19 virus cycle threshold (CT) value corresponding to viral load and age, CRP, lymphocyte, neutrophil, platelet, AST, ALT, ferritin, LDH. The significance level was accepted as $p<0.05$ in all analyzes.

Ethical Approval

Ethics Committee approval for the study was obtained.

Results

The median age of the patients included in the study was 64 (14-90) years. Of the 85 patients with positive COVID-19 RT-PCR test, 43 (50.58 %) were mild/moderate and 42 (49.2 %) were severe/critical. Thirty-five (41.2 %) of the 85 participants had chronic disease (Table 1).

The most common underlying diseases in the severe/critical patient group were hypertension (20%), followed by chronic

Table 1. Demographic and Biochemical characteristics of COVID-19 patients according to the severity of the disease

			Mild/Moderate	Severe/Critical
		n:85	43 (%50,48)	42 (%49,52)
Woman		n:45 (%52)	25 (%55)	20 (%44)
Male		n:40 (%48)	18 (%45)	22 (%46)
Age		64 (14-90)	45 (14-77)	71 (33-90)
Median (min-max)	ALT (U/L)	21 (5-205)	20 (5-150)	23 (7–205)
	AST(U/L)	26 (10-607)	24 (12-125)	30 (10-607)
	CRP (mg/L)	34 (3-228)	3,14 (3-199)	66 (3-228)
	LDH (U/L)	273 (89-1219)	200 (89-526)	417 (153-1219)
	Neutrophils (µL)	5 (0-26,8)	3,4 (0-15,3)	8,6 (2,6-26,8)
	Lymphocytes	0,8 (0-3,7)	1,3 (0-3,70)	0,5 (0,2-2,90)
	Ferritin (µg)	115 (3,8-1500)	58 (3,8-1500)	275 (4,5-1500)

Table 2. Comparison of CT values of COVID-19 patients with prognosis

		CT Value mean ± sd	Test value	p
Disease Severity	mild/moderate	23.40±5.28	-0.493*	0.623
	severe/critical	24.02±5.36		
Mortality	yes	24.02±5.79	0,868*	0.388
	no	22.75±5.93		
Hospitalization	yes	23.94±5.84	0.879*	0.382
	no	22.40±5.75		
Comorbidity	yes	24.19±5.53	0,641*	0.524
	no	23.37±6.04		
Intensive care unit	yes	24.11±5.33	0.649*	0.518
	no	22.29±6.32		

*Student T-Test

heart disease (18.8%). Chronic diseases appear to be more common in patients with severe COVID-19. The mean PCR CT value of the participants was 23.71±5.82.

As a result of Pearson's correlation analysis, it was determined that there was no relationship between the biochemical parameters of the participants included in the study and the COVID-19 virus cycle threshold (CT) value corresponding to the virus load (p>0.05).

No correlation was found between disease severity, vital status, hospitalization in the hospital or intensive care unit, presence of comorbidity, and mean CT values (p>0.05) (Table 2).

Discussion

The main result of our study is that ΔCT, which is assumed to be inversely related to viral load, could not be found to be significantly associated with baseline values and disease severity in adults with COVID-19.

Muhammad et al. in their study, in which they grouped CT values and compared them with disease severity, found no statistical significance, similar to our study [8]. However, there are publications in the literature showing that the viral load of the sputum sample in the lower respiratory tract that was initially tested is closely related to the severity of COVID-19 [9,10]. In our study, in accordance with the literature, the severe/critical patient group consisted of more advanced age groups [11]. Similar to our study, Waleed et al. could not detect a statistically significant difference between age and viral load in their study [12]. Wenyu Chen et al. in their study suggested that an increased viral load may be the key factor leading to the overload of the body's immune response and causing the disease to progress to a serious illness [7].

A study on children with COVID-19 showed that patients had a similar amount of viral load across all disease processes, similar to our adult group, regardless of age and underlying disease [13].

Some studies suggest that the classification of SARS-CoV-2 positive cases according to CT values can be used to determine contagiousness, isolation at home or discharge from the hospital [14,15].

The main limitation of our study is the inability to perform serial sampling for PCR and viral load due to its retrospective nature. It would be better to evaluate viral dynamics by serial sampling with more patients and considering many different variables. During the Sars Cov 2 pandemic, many variants have emerged. There were no variant results in the system from which the data were obtained. The disease severity in patients infected with different variants may also be different.

As a result, positive or negative SARS-CoV-2 test results are sufficient for diagnosis; however, additional supporting data and prospective studies are needed on whether CT values can benefit clinicians in clinical and patient management decisions.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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Conflict of interest

The authors declare no conflict of interest.

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